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Serum free L-carnitine in association with myoglobin as a diagnostic marker of acute myocardial infarction

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Abstract

Background: Early diagnosis of acute myocardial infarction (AMI) in patients with chest pain is necessary to initiate appropriate treatment. Elevation of ST-segment in ECG is the only marker that cardiologists depend on in diagnosis. The aim of this study was to monitor the level of serum free L-carnitine in combination with myoglobin (Myo) and creatine kinase (total activity and CK-MB level) for usefulness as a predictor of AMI in ICU patients.

Design and methods: In the present study serum total CK activity and CK-MB, Myo, and free L-carnitine levels were determined in 90 patients admitted to the ICU at Ain Shams University Hospital and correlated the sensitivity and specificity of each parameter.

Results: Obtained data revealed that, 47/90 who were diagnosed as AMI showed a highly significant reduction in serum free L-carnitine level in all cases as compared to normal control ($P<0.001$), 24/90 diagnosed as unstable angina showed a non significant reduction of serum carnitine and 19/90 who were diagnosed as noncardiac showed non significant changes in the level of serum free carnitine as compared to normal control. In addition, serum free L-carnitine level was negatively correlated to CK-MB and Myo ($r=-0.61$ and -0.52) respectively. The sensitivity of carnitine assay was considerably higher (95.5%) compared to CK-MB (87%) and Myo (89.5%) even considering patients with a short delay until admission.

Conclusion: Comparing the changes in serum total CK, levels of CK-MB, Myo and carnitine, the sensitivity and specificity were significantly higher for serum free L-carnitine. For this reason, serum free L-carnitine can be used as a good predictor for AMI diagnosis from other diseases.

Keywords: Acute myocardial infarction; L-carnitine; Myoglobin; CK-MB

Introduction

The most typical electrocardiogram (ECG) indicating acute myocardial infarction (AMI) is elevation of ST segment and these patients will in a high percentage develop AMI [1]. ECG is the first assessment in patients presenting at an emergency unit with chest pain suggesting acute coronary syndrome. However, among high percentage of patients without ST segment elevation, there are no strong predictors of the development of AMI. The biochemical markers play an important role in early diagnosis of AMI. Two of the oldest markers of AMI, asparate aminotransferase (AST) and lactate dehydrogenase (LDH) are still in use in some laboratories but they have little value as markers of cardiac dysfunction and have been superseded by newer markers [2].

Serum total creatine kinase (CK) and creatine kinase-MB (CK-MB) are commonly used as biochemical markers of myocardial injury that aid in the risk stratification of the heterogeneous group of patients evaluated for chest pain [3]. Myoglobin is a small (17.8 kD) cytoplasmic heme protein found in all muscles. Myoglobin increases within 1 to 3 h in the setting of myocardial necrosis, usually peaks within 6 to 9 h, and may become normal in 24 h [4].

Carnitine (L-3-hydroxy-4-N,N,N-trimethylaminobutyrate) is an essential metabolic mediator, which has a number of indispensable roles in intermediary metabolism [5]. It has important roles in fatty acid metabolism, as well as in carbohydrate oxidation in cardiac myocytes, including facilitating β-oxidation by transporting activated fatty acids into the mitochondrial matrix

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[6]. In humans, the carnitine supply is derived in part from food and in part by endogenous synthesis from lysine and methionine [7]. Exogenous L-carnitine is used clinically for the treatment of carnitine deficiency disorders and a range of other conditions [8].

The ability of the cell to utilize fatty acids as a source of fuel is essential for optimizing the production of ATP by mitochondria in cardiac cells to keep the heart properly functioning. L-carnitine assists in this transportation process by bringing fatty acids from the extracellular space into the mitochondria [8].

The goal of the present study is to evaluate serum free-L carnitine level in combination with total CK, the levels of CK-MB and Myo in admitted ICU patients to be utilized as a diagnostic marker of AMI patients and differentiated from other diseases with a suspicion of an acute coronary syndrome with and without ST elevation on the admission ECG. Secondly we will correlate the results obtained with the other markers for predicting sensitivity and specificity to assist physicians in fast diagnosis and early treatment of AMI.

Subjects and methods

Subjects

The study protocol was approved by the local ethics committee. A written informed consent was obtained from each subject.

This study included 90 non consecutive patients; 70 males and 20 females, age ranged (35–62), mean ± SD (61 ± 15.5 years) suffering from chest discomfort or other symptoms raising a suspicion of an acute coronary syndrome reached to the ICU at Ain Shams University Hospital between October 2006 and May 2007. The time interval between the onset of pain and ICU admission was 4 h. In addition 15 normal subjects whose age and sex matched, and free from any diseases as, hypertension, diabetic, renal, metabolic disorder and any history of cardiac disease were selected as control. Blood samples were collected on admission, centrifuged for 10 min at 4000 rpm. Sera were stored at −70 °C until analysis. The protocol was approved by fully informed consent obtained from each subject studied.

Enrolment criteria include chest pain or chest discomfort for more than 15 min within the last 6 h, dyspnea without known lung disease such as asthma or bronchitis. Previous history of myocardial infarction, angina pectoris, hypertension, diabetes, congestive heart failure and smoking were excluded.

An acute myocardial infarction has a criterion for ECG changes, ST elevation: z2 mm in leads V1–V4, z1 mm in leads V5–V6 and in any of the extremity leads. ST depression: z1 mm in any lead.

Methods

Total serum CK activity was determined using *N*-acetyl-cysteine activation without pretreatment while CK-MB and myoglobin levels were assayed by the method described in [9].

Serum L-carnitine level was measured by an enzymatic spectrophotometric assay according to the technique of Marquis and Fritz [10]. Briefly, 1 mL of 100 mmol/L Tris–HCl buffer (pH 9.5), 5 mmol/L thio-NAD^+, 0.2 mmol/L NADH, and 100 kU/L carnitine dehydrogenase in a 10 mm path-length cuvette for 3 min and 1 kU/L acylcarnitine hydrolase were incubated at 37 °C. Then, the increasing rate of thio-NADH, which is proportional to the amount of L-carnitine, was measured from absorbance at 415 nm during a time interval of 1 to 6 min after the addition of 50 μL of the serum specimen or L-carnitine standard solution. The concentration of L-carnitine was calculated on the basis of a comparison with the rate obtained with a 50 mmol/L L-carnitine standard solution.

Statistical analysis

Results were expressed as mean ± SD. Sensitivity was calculated as: (patients with positive markers and AMI)/(all patients with AMI); specificity was calculated as: (patients with negative markers without AMI)/(all patients without AMI). Results were compared using Student's *t* test for continuous variables and chi-square analysis for dichotomous variables. A P value ≤ 0.05 was considered significant. One-way ANOVA was additionally used as a confirmatory test, complemented by Tukey's test to discover significant intergroup differences. Wilcoxon test was also applied as a non parametric significance test. Receiver operating curve (ROC) analysis was used to calculate the diagnostic accuracy of each marker.

Results

Clinical examination revealed that, (61.6%) of patients had a final diagnosis of acute myocardial infarction, (23.4%) had a diagnosis of unstable angina and 15% had a final diagnosis of

Table 1
The activity of serum total creatine kinase (CK) and the levels of creatine kinase (CK-MB), myoglobin, and free L-carnitine in all studied groups (mean ± SD)

Patients groups	Normal control n = 15	AMI n = 47	Unstable angina n = 24	Noncardic diseases n = 19
Parameters				
Total CK (U/L) mean ± SD	120.8 ± 23	490 ± 56[a***]	312.7 ± 25.8[a***, b***]	139.3 ± 28.2[a N.S., c***]
CK-MB (ng/mL) mean ± SD	59 ± 11	94 ± 19[a***]	61.5 ± 14.9[a N.S., b***]	51 ± 8.4[a N.S., c***]
Myoglobin (ng/mL) mean ± SD	40.1 ± 5.4	179 ± 23.7[a***]	99 ± 23.8[a***, b*]	48 ± 6.5[a N.S., c**]
Free L-Carnitine (mmol/L)	42.4 ± 6.1	25.7 ± 2.8[a***]	36.8 ± 4.3[a N.S., b***]	41.6 ± 5.08[a N.S., **]

*P < 0.05; **P < 0.01; ***P < 0.001.
[a]AMI, unstable angina and noncardiac vs control.
[b]AMI vs unstable angina.
[c]AMI vs noncardiac.